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The reaction of the blood

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# THE REACTION OF THE BLOOD.[1]

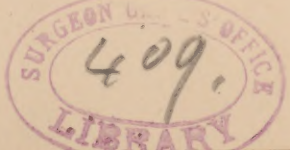
BY JOHN A. JEFFRIES, M.D.

WHILE much attention has been paid to the formed elements of the blood, but little comparatively has been given to its chemistry. The first question to suggest itself from this side has received but a sparing amount of attention in Europe and none at all in America. I refer to the reaction of the blood. We read that the blood is alkaline and that is about all. To be sure, we hear much about an acid diathesis in rheumatism and gout, unsupported in the first case by any evidence. In gout Garrod has clearly showed the part played by uric acid, that is, its prevalence in the system and especially in the affected parts.

While working in the Pathological Institute of Vienna from the winter of 1884 to 1886, I was struck by the peculiar general distribution of the tubercle bacillus, as represented by tubercular products found at autopsies.

One or another of the products of tuberculosis were to be found in the majority of the subjects which came to the table, and this in spite of the fact that those known to be dead of phthisis mostly went to the anatomical department. Yet tuberculosis of the muscles is relatively rare; it is by no means easy to procure examples of tuberculosis in muscular tissue for microscopic preparations.

[1] Read before Boston Society of Medical Sciences, March 19, 1889.



Pathological changes are to be found, due, as E. Fränkel points out, to the general effects of the disease, but the bacillus is not so easily found. The same is true of the stomach and to a less but distinct degree of the genito-urinary tract. In any case of acute miliary tuberculosis the little glistening, transparent tubercles are to be found scattered along the blood-vessels throughout the rest of the body.

Why this difference? Why are organs of such diverse structure as the mucosa of the stomach, the muscles, and the genito-urinary organs comparatively exempt? It might be said that the histology of the muscles was very distinct from that of other parts, and so not adapted to the development of tuberculosis; but the same cannot be said of the stomach, while the mucosa of the intestines is so often radically affected.

These parts have, nevertheless, one character in common which separates them broadly from the rest of the body. They are exposed to an acid reaction. During a good part of the time the mucosa of the stomach is bathed in an acid juice secreted by itself; the same is true of the urinary tract and of the muscles. The urine is mostly acid in reaction, the muscles change during action from an alkaline to an acid reaction. This is easily shown by inserting bits of litmus paper in any relaxed muscle; the red bits become blue. Now cause sharp contractions by applying a faradic current to the nerve above, and the blue paper will shortly turn back to red.

As opposed to this, all know that as a general law bacteria grow poorly or not at all on media of animal origin with an acid reaction, and any one who has grown the tubercle bacillus knows that it forms no exception to the rule. The bacteri-

ologist who neglects the reaction of his media will soon have cause to rue.

Putting these two together the question, Is the reaction of the tissues one of the leading causes of the distribution of tuberculosis, naturally presents itself and may in a general way be extended to the whole group of infectious disease.

To investigate this, naturally brought up the question as to the reaction of the blood: could it be changed and does it vary in different kinds of animals?

On returning from Europe during the latter part of 1886 and first part of 1887 I took up the subject in co-operation with Dr. James J. Putnam. Later, by pressure of more urgent work and the difficulties inherent to all scientific work in this country, we were both of us driven from the subject. At this time we stood alone in the question, and Dr. Putnam was inclined to believe, in view of Meyer's work, that our methods could not give any reliable results. As, however, the subject has been since taken up by Jaksch,[2] it seems to me that a report of our methods and results on testing the reaction of blood may not be without interest.

Of the chemical composition of the blood little if anything is known. We have analyses of the ash of the corpuscles and serum, and the elements in them, but how these are combined is a matter of speculation. We are therefore dealing in reality with an unknown mixture.

To test the reaction of the blood two different methods have been pursued, one by the direct use of litmus or other indicator, the other by inference from the amount of carbon dioxide that can be extracted by the air-pump, either alone or with the

[2] Jaksch. Ueber die Alkalescenz des Blutes bei Krankheiten. Zeitschrf. f. klin. Med., 1887, p. 350.

addition of a certain amount of acid, usually phosphoric. We pursued the direct method.

A moment must be given to what this method gives us. All reagents as to reaction are merely indices, and do not run, as many seem to suppose, parallel to each other and chemical composition. The parallelism is only general, not absolute. Of these indices litmus seemed to be the best adapted to our purposes. It shows both actions, acid and alkaline, distinctly, can be used on paper, and is fairly sensitive.

Alkaline bases turn the color blue, and acids red, if they act. Some, as uric acid, act as neutral bodies —have no effect on the color. Salts follow more or less closely after their composition: thus most acid salts turn the paper red, alkaline ones blue, while still other are neutral, have no effect. But this is not invariably the case: bicarbonate of soda is an acid salt, that is, the acid element is not satisfied, is capable of joining with more base, yet its reaction is that of an alkali to litmus, which it blues strongly.

In this paper, therefore, in common with all others who have written on the subject, by alkaline is meant the property to blue litmus.

Owing to the hæmoglobin and the coagulation of the blood when drawn from the body, testing the reaction offers peculiar difficulties, and various expedients have been resorted to. Thus Kuhne[3] tried to separate the fluid by means of dialyzation; Liebreich[4] and others used a very thin plate of pure gypsum, through which the serum of the blood passed, and could be tested either by litmus paper

[3] Kuhne. Die einfaches Verfahren die Reaction hämaglobinhaltiger Flussigkeiten su prüfen. Virchow's Archiv, xxxiii. p. 95, 1865.

[4] Liebreich. Eine Method sur Prüfung der Reaction thierische Gewebe. Berichte der deutsch. chim. Gesellsch. zu Berlin, 1868, p. 48.

or directly by previously soaking the tablets in a neutral solution of litmus. Lassar,[5] Canard,[6] Mya and Tassinari,[7] Landois,[8] and von Jaksch all used litmus paper, some noting reaction from the part soaked beyond the clot, others washing the blood off. At times the paper was previously moistened with a salt solution to keep the hæmoglobin off.

To prevent coagulation the blood has by most recent observers been mixed with a neutral 10% solution of sulphate of soda.

As an acid for titration phosphoric,[9] tartaric, and oxalic have been used in very weak solution. Phosphoric is ill adapted, since in small quantities it gives but a poor reaction with litmus; the salts are often amphoteric. Oxalic I have distrusted on account of its strong affinity for lime.

The blood has been drawn in various ways, either in considerable quantities from the arteries of animals, or a few cubic centimetres from the finger in man by means of a lancet, or a drop from a needle prick, as practised by Landois.

Landois and von Jaksch used a large number of solutions of sulphate of soda *plus* a given amount of acid, and added a definite amount of blood by means of a pipette, and then noted, after stirring, which was neutral; read off the acid strength. The other authors slowly added the acid solution and tested from time to time. This is inadmissible, since the blood diminishes in alkalinity very rapidly after being drawn. All have used a small amount of

[5] Lassar. Zur Alkalescenz des Blutes. Pflüger's Archiv, ix. p. 44, 1874.

[6] Canard. Essaie sur l'alcalinité du Sang dans l'état du sante et dans quelques maladies. Paris, 1878.

[7] Mya, Tassinari. Sulle variazioni della reazione alcalina del sangue venoso. Archiv per le scienze mediche, ix. p. 379, 1886.

[8] Landois, Real-Encyclopädie der gesammten Heilkunde, 2 Aufl. iii. p. 161, 1885.

[9] Zuntz. Zur Kenntniss des Stoffwechsels im Blute. Centralb. f. d. med. Wiss., 1867, p. 801.

blood, but agree that the results are the same as with larger quantities.

The method used by us, worked out in the rough by Dr. Putnam before I joined him, is as follows:[10] A small drop, .02 c.cm., of blood taken from a drop produced by a prick of the back of the finger is mixed with a given quantity of a standard dilute solution of tartaric acid and all then placed on a piece of very smooth-painted, dry litmus paper. This is then washed off in neutral water, and the color, where the drop has been, noted. As a rule both colors of litmus papers were used. The whole process takes from fifty to ninety seconds. If the first test does not come out right, a second, with more or less acid as indicated, is to be made.

As our experience increased the method was perfected and various sources of error eliminated. It may therefore be well to give the whole in detail.

Our pipettes are made from a piece of thermometer tubing of rather coarse bore, ground to a point at one end, from which marks at definite intervals, each equal to about .01 c.c., run, up to twenty. On the other end is slipped a piece of rubber tubing about three inches long and stopped by a solid, glass rod. By means of this rubber tube any desired amount of fluid can be drawn up into the tube and the end then dried with a bit of absorbent cotton.

The acid solution is made by taking a $\frac{1}{5000}$ solution of corrosive sublimate and adding sufficient pure crystalline tartaric acid, so that fifteen parts of the acid solution exactly neutralized eight parts of the volumetric solution of soda of the United States Pharmacopœia diluted with thirty-nine times its bulk of water. The acid salt of mercury is added to prevent the growth of the lower plants, which otherwise quickly occurs.

[10] This method is similar yet distinct from that of Landois, and more portable.

From six to seven measures of this acid solution are drawn into the tube and well up, the lower six being left empty, and the tip of the pipette dried.

Around the second joint of the finger, carefully cleaned, a light rubber band is passed, and a prick with a surgical needle made in the back of the last phalanx behind the quick of the nail. From the drop of blood which quickly comes two measures are drawn into the pipette, and the tip wiped with cotton. Then blood and acid are squirted into a small vial and mixed by rapid alternate sucking and squirting of the pipette. Lastly, the mixture is drawn up and deposited on bits of the litmus paper previously pinned onto corks. At the end of five seconds the corks and paper are plunged into water and the color noted.

The whole is to be done in much less time than it takes to describe it, and is quite accurate. The acid can be measured off at leisure: haste only comes after the blood is drawn. Any slight surplus of blood can be quickly removed by a pledget of absorbent cotton. Some sources of confusion are to be noted. The blood is bright red; therefore if the observer gazes intently at it while on the paper, he will after washing it off see the complementary color, irrespective of the color of the paper. This is really nothing but an experiment on negative after-images which is out of place. Again the observer must be careful, especially if near-sighted, not to breathe upon the paper, as it will quickly become affected by the carbonic acid expired by the lungs. The test paper must be handled with clean forceps, not touched by the fingers, which are acid and will affect it; the same is true of almost any moist vegetable product, such as wood.

The color of the paper must be promptly noted, since it fades on standing.

This method is accurate, and I believe gives us about all that is to be gathered concerning the direct reaction of the blood. Over the older methods it has the advantage of being applicable time and time again to anybody, as the writer knows by personal experience, and portable.

It gives about fifteen different degrees of alkalinity between a neutral reaction and the higher alkaline reactions noted. From the known ratio of blood and acid used the amount of acid required to neutralize 100 c.cm. of blood can be quickly counted. Thus, if two parts of blood and seven of acid are used we have 100 c.cm. of blood = 350 c.cm. of acid = $\frac{350 \times 8}{15 \times 4.0}$ of volumetric solution of soda = 4.6 = .186 gramme of pure NaOH. As the blood can be made a fixed quantity, two parts, a working table as given below can be made, where the first number is the number of acid parts taken and the last the amount of alkalinity measured by NaOH. in 100 c.cm. of blood.

| Parts of Acid. Sol. | Parts of Na. Sol. | Na. in mg. To 100 c.cm of Blood | Parts of Acid. Sol. | Parts of Na. Sol. | Na. in mg. To 100 c.cm of Blood |
|---|---|---|---|---|---|
| 1 | .53 | 26 | 7 | 3.73 | 186 |
| 2 | 1.06 | 53 | 8 | 4.26 | 213 |
| 3 | 1.60 | 79. | 9 | 4.80 | 240 |
| 4 | 2.13 | 106 | 10 | 5.33 | 266 |
| 5 | 2.66 | 133 | 11 | 5.86 | 293 |
| 6 | 3.20 | 160 | 12 | 6.40 | 320 |

It is to be noted here that Meyer,[11] a strong advocate of the $CO_2$ method of determining the alkalinity, has strongly attacked all efforts to determine the

[11] Meyer. Studien über die Alkalescenz des Blutes. Archiv f. exper. Path. u. Pharm., xvii. p. 304, 1883.

reaction by direct testing. He points out that the blood is of unknown composition, hence we do not know what we are dealing with; and, second, that many complex substances do not act on litmus as indicated by their chemical affinities.

While not claiming that any direct method gives an absolute measure of the bases, it seems to the writer, in common with von Jaksch and others, that the measure of alkalinity as directly observed is of value from both clinical and physiological standpoints.

We do not know just what the blood is composed of, but we do know that it is pretty much the same thing all through air-breathing vertebrates, and is therefore fairly comparable.

The other objection, as pointed out by Mya and Tassinari, is a play on words. Nobody for an instant supposes that in measuring the reaction of a complex mixture he is obtaining an absolute measure of the alkaline or acid bases, as defined by chemical philosophy, which remain unsatisfied, but knows he is making an empirical observation of the degree of reaction as indicated by the index used.

The true objection rests in the fact that the blood begins to lose its alkaline reaction very shortly after being drawn. Empirically, however, it can also be shown that but little diminution occurs in the first ninety seconds, when mixed with the acid mixture used. The corrosive sublimate tends to hold the blood unaltered.

As for the $CO_2$ method, it is, for general application, utterly out of the question. It does not give any idea of the quantity of unsatisfied bases, and is based on a whole train of suppositions. Reducible to the fact that no other explanation of the retention of the $CO_2$ in the blood has been given than a grip exerted by the unsatisfied bases, and the fact

that acids fed to animals reduce the $CO_2$ in the blood, presumably by satisfying the bases.

In defects the method is rich, among them the fact that the $CO_2$ in the blood is much influenced by the respiration, entirely independent of the alkaline bases present, as shown by Minkowski.[12]

In spite of this the method is of value, and to the writer's thinking both methods are increased in value by the fact that the results obtained by careful observers by the two methods closely coincide.

In studying the alkalinity of the blood we have but varying degrees of reaction to compare,— possibly at times a change to acidity just before death, — that is, changes in quantity only. Qualitative changes are only to be got in changes of condition of the animal observed. Thus poisons, complete change from natural diet, and the like, may be made. Again the urine requires careful attention as being the chief scape-vent for the blood, and therefore influenced by the varying conditions of the blood. But the first step is to acquire an idea of the normal conditions of the blood, and its relations to the urine and food, time of day, age, and sex.

In determining normal conditions the $CO_2$ method is of very little value: continuous observations cannot be made, and the operation of bleeding throws the animal at once out of normal conditions. This is not true of our method: a simple prick does no harm, and the experiments can be conducted upon man.

The figures of Meyer, Feitelberg,[13] and Minkowski run, for each kind of animal tested, within a 30% limit of variation, and making due allowances for differences in the complex technique, justify their

[12] Minkowski. Ueber den Kohlensäuregehalt des arteriellen Blutes beim Fieber. Archiv f. exper. Path. u. Pharm.

[13] Feitelberg. Ueber den Einfluss einige Gifte auf die Alkalescenz des Blutes. Diss. Inaug. Dorpat, 1883.

assumption of a normal standard of $CO_2$ in the blood. By the direct method Lassar, Mya and Tassinari, and Canard have endeavored to find standards, — the first in rabbits and cats, the last two authors in man. Reduced to a common standard Lassar found —

| | | | | | |
|---|---|---|---|---|---|
| German rabbits, 100 c.cm. of blood = | ..... | .188 | NaOH. |
| French " " " " | ..... | .212 | " |
| Cats, " " " " | ..... | .241 | " |

the variations being within 15 per cent. from the mean. Mya and Tassinari place the average in man at .4, a figure much higher than those of any other observer. Canard gives .228 as the average, .272 as the maximum, and .203 as the minimum of fourteen healthy adults. My own figures run constantly much lower: thus rabbits at .160; frogs at .70; hens at .200; man, from 5 healthy individuals and one hundred observations, at about .200. max. .259; min. .160. Von Jaksch figures in disease from .036 to .350.

These figures, it will be seen, are very different from one another, and preclude all deductions as to quantity. They, however, in the case of each observer, give relatively similar results. These differences are doubtless due to the different acids used, the nature of the blood, arterial or capillary, the time the blood had been drawn, and the quality of the litmus paper. Ordinary litmus paper, such as most of the authors used, contains a good deal of acid or alkali, which tends, when using small quantities of blood, to greatly increase the reading.

My own observations have so far been directed to ascertaining the normal standard, and especially any variations, diurnal or from day to day. Below is given a set of figures, taken from one person, reduced to milligrammes of NaOH to 100 c.cm. of blood. B, L, and D denote the last meal. Breakfast at

| | | | | | |
|---|---|---|---|---|---|
| 9.30 A.M. | 8/8 | 86 | B | 175 | |
| 2. P.M. | | | B | 226 | |
| 6 P.M. | | | D | 175 | |
| 8 A.M. | 9/8 | | B | 175 | |
| 11.30 | | | B | 175 | |
| 3.30 P.M. | | | B | 245 | |
| 2.30 P.M. | 10/8 | | B | 245 | |
| 3.30 P.M. | 11/8 | | L | 210 | |
| 3 P.M. | 13/8 | | B | 245 | |
| 12 Noon | 15/8 | | B | 280 | |
| 3 P.M. | 17/8 | | L | 199 | |
| 2 P.M. | 30/8 | | L | 173 | |
| 8.30 A.M. | 31/8 | | Fast | 160 | |
| 8.30 A.M. | 2/9 | | " | 160 | |
| 2. P.M. | 8/9 | | L | 186 | |
| 5 P.M. | 8/9 | | L | 213 | |
| 2 P.M. | 9/9 | | L | 186 | |
| 2 P.M. | 10/9 | | L | 213 | |
| 11.30 A.M. | 11/9 | | B | 160 | |
| 1 P.M. | 11/9 | | B | 226 | |
| 3 P.M. | 11/9 | | B | 250 | |
| 4.30 P.M. | 11/9 | | D | 200 | |
| 8.30 A.M. | 13/9 | | B | 250 | |
| 1.45 P.M. | 13/9 | | L | 240 | |
| 11 A.M. | 1/10 | | B | 213 | |
| 9.30 A.M. | 3/10 | | B | 200 | |
| 2 P.M. | 3/10 | | B | 213 | |
| 9 A.M. | 3/10 | | B | 173 | |
| 12 M. | 3/10 | 86 | B | 186 | |
| 11.30 A.M. | 4/10 | | B | 186 | |
| 2. P.M. | 4/10 | | B | 226 | |

7 A.M., lunch at 1. P.M. when taken. The regular dinner hour was 7 P.M., too late for observations to be made after it. On the two occasions where D is put down it was taken earlier in the afternoon.

The above figures look rather formidable, but with a knowledge of the life of the observer seem to clearly show one general rule, namelo, a gradual rise in the reaction from rising to before dinner. Thus the average on rising is .155; between 9 and 11 A.M. .189; between 1 and 3.30 P.M., with lunch, .191: without lunch, .212. These averages include all the figures where a regular life was being led, including about five miles of walking and the ordinary

| | | | | | |
|---|---|---|---|---|---|
| 9.30 | A.M. | 5/10 | B | 250 | work of an out- |
| 2.30 | P.M. | 5/10 | B | 213 | patient service. |
| 9.20 | A.M. | 6/10 | B | 186 | The fact that the |
| 2 | P.M. | 6/10 | B | 186 | reaction was |
| 9.20 | A.M. | 7/10 | B | 213 | higher in the early |
| 2 | P.M. | 7/10 | B | 200 | afternoon of days |
| 10 | A.M. | 8/10 | B | 186 | when no lunch was |
| 2 | P.M. | 8/10 | B | 213 | taken than when |
| 11. | A.M. | 9/10 | B | 213 | lunch was taken is |
| 2 | P.M. | 9/10 | B | 186 | of interest; also |
| 9 | A.M. | 10/10 | B | 186 | the two measure- |
| 10 | A.M. | 10/10 | B | 186 | ments taken after |
| 0.15 | P.M. | 10/10 | B | 160 | dinner, which show |
| 2.50 | P.M. | 10/10 | L | 160 | a lower reaction |
| 9.15 | A.M. | 11/10 | B | 186 | than before dinner. |
| 2 | P.M. | 11/10 | B | 200 | These two facts |
| 9.30 | A.M. | 12/10 | B | 186 | seem to stand in |
| 2.10 | P.M. | 12/10 | L | 186 | direct opposition |
| 11. | A.M. | 13/10 | B | 186 | to Canard's and |
| 2 | P.M. | 13/10 | B | 186 | Sticker and Heu- |
| 1.20 | P.M. | 14/10 | B | 213 | ber's [14] observa- |
| 2 | P.M. | 15/10 | B | 213 | tions, who found |
| 11 | A.M. | 16/10 | B | 186 | that the alkalinity |
| 2.15 | A.M. | 16/10 | B | 213 | rose after meals. |
| 9.15 | A.M. | 17/10 | B | 186 | The rise they at- |
| 2. | P.M. | 17/10 | B | 130 | tribute to the loss |
| 9 | A.M. | 18/10 | B | 213 | of the hydrochloric |
| 2 | P.M. | 18/10 | B | 213 | acid poured into |
| 9 | A.M. | 19/10 | B | 240 | the stomach. |
| 7 | A.M. | 28/10 | | 146 | Canard's figures |
| 9.30 | A.M. | 28/10 | B | 173 | I cannot explain; |

those of Sticker and Heuber were done by Zuntz' method with phosphoric acid, which is unreliable, and

Sulphate of quinine was taken in ten-grain dose on 10-10 at 9.15 A.M., and 17-10 at 10 A.M.

[14] Sticker u. Heuber. Ueber Wechselbeziehungen zwischen Secreten und Excreten des Organismus. Zeit. f. klin. Med., Bd. 12, p. 136 foot-note.

| | | | | | |
|---|---|---|---|---|---|
| 11. | A.M. | 25/10 | | B | 186 |
| 2.15 | P.M. | 25/10 | | L | 200 |
| 7.20 | A.M. | 5/11 | | Asst | 160 |
| 10. | A.M. | 5/11 | | B | 213 |
| 2 | P.M. | 5/11 | | | 226 |
| 10 | A.M. | 10/11 | | B | 186 |
| 2 | P.M. | 10/11 | | | 213 |
| 2.30 | P.M. | 10/12 | | L | 186 |
| 10.45 | A.M. | 30/1 | 87 | B | 186 |
| 12, | Noon | 30/1 | | B | 146 |
| 1.30 | P.M. | 30/1 | | B | 146 |
| 10 | A.M. | 5/2 | | B | 173 |
| 0.30 | P.M. | 5/2 | | B | 146 |
| 0.10 | P.M. | 11/2 | | B | 186 |
| 2. | P.M. | 11/2 | | L | 146 |
| 4 | P.M. | 11/2 | | L | 120 |
| 10 | A.M. | 22/2 | | B | 200 |
| 1. | P.M. | 22/2 | | B | 186 |
| 1.45 | P.M. | 22/2 | | B | 173 |
| 2.45 | P.M. | 22/2 | | L | 173 |
| 3.40 | P.M. | 22/2 | | L | 186 |
| 845 | A.M. | 1/3 | 87 | B | 186 |
| 11.20 | A.M. | 1/3 | | B | 186 |
| 1. | P.M. | 1/3 | | B | 186 |
| 5. | P.M. | 1/3 | | L | 160 |

R. ab hit.

| | | | | | |
|---|---|---|---|---|---|
| 11. | A.M. | 14/2 | | | 160 |
| 10.30 | A.M. | 29/2 | | | 160 |
| 11.30 | A.M. | 29/2 | | | 133 |
| 1.20 | A.M. | 29/2 | | | 120 |

Antifebrin was taken in four-grain doses 31-1, 87, 10.47 A.M.; 5-2, 10-10 A.M.; 11-2, 12.30, and 2 P.M.; 22.2, 10-10 A.M. and 1 P.M.; 13.3, 8-45, 11.20, and 2.20.

the time of day is not given; they may therefore have been dealing with the early morning rise, which is clearly due to the more active life. As the reaction of the chyme in the intestines is alkaline, it is just as reasonable to assume that the blood should be reduced in reaction during digestion, especially as absorption is rapid and the result of ordinary food on the acid side.

The reaction of the blood the writer believes to be of considerable importance to the economy, and therefore not very variable in perfect health.

Noting the fact that the alkalinity was very apt to be high at times when headache over one or both eyes, with tenderness of the

nerves, existed, tests were made with two of the drugs found to relieve the pain. Sulphate of quinine in ten-grain doses was found in three trials to depress the reaction as noted. The same was true of antifebrin in five trials. As the normal tendency of the reaction was to rise during the time of these experiments, it seems highly probable that the observation is correct. Perhaps the headaches were gouty in nature.

The reaction of the blood in poisoned animals, as indicated by the amount of $CO_2$, has been studied by several observers, and found to be diminished in septic fever, iodin, mercury, nitrite of soda, toluylendiamin, oxalate of soda, and strychnine poisoning. Alcohol and salicylate of soda apparently increase it.

In disease the writer regrets that he has been unable to procure sufficient material. Several writers, however, have turned their attention in this direction. There are many old records of the blood being acid in cholera and leukæmia, but most have been taken from the corpse and so are worthless. Cantani claims to have found the blood acid in advanced cholera cases during life, and Mya and Tassinari state that this was found to be the case in Naples during the last epidemic. The method of determining the reaction is not given in either case.

Canard found the reaction increased in acute and subacute articular rheumatism (it is not clear if salicylate of soda was given), and diminished in arthritis deformans. Diabetes mellitus and cancer of the stomach also showed a diminution.

Mya and Tassinari found the reaction increased in pneumonia, treated by baths and stimulants, diminished in typhoid, cancer, phthisis, Bright's, diabetes, oligæmia, and chlorosis.

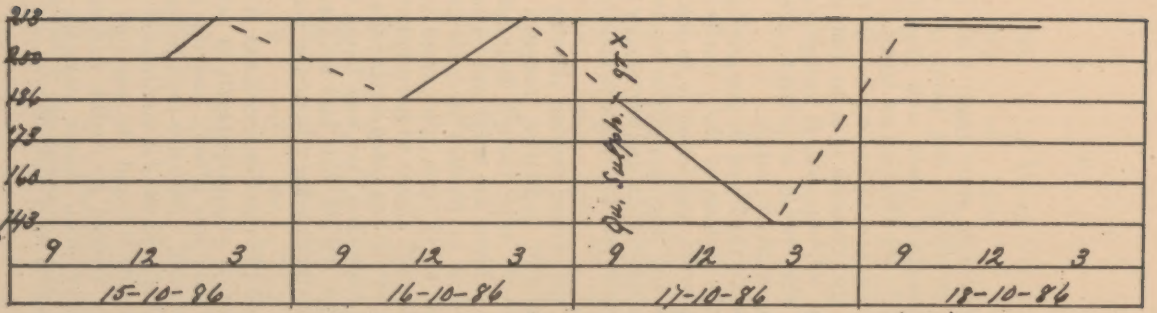



Chart showing effect of quinine

Jaksch has made by far the most extensive study of the subject, and found a distinct diminution in the reaction during fever, quickly recovering after it. The most marked changes were found in uræmic poisoning, destructive diseases of the liver, and leukæmia, where the blood becomes almost neutral. The other blood diseases offer a less marked diminution.

How the standard is maintained in the blood is not thoroughly known. But in normal conditions animals maintain an alkaline reaction against the final result of the ingesta, which result in an acid surplus. The acid is thrown off by the lungs ($CO_2$) and in the urine. The weight of evidence seems to be that the acid does not go through the blood as such, but combines and is separated in the kidneys in part, in part goes out as a whole. Therefore by feeding with sulphuric acid it is possible to materially reduce the alkali in the blood; that is, rob the system, of course with disastrous results. Under these conditions much ammonia appears in the urine of carnivora but not in the urine of herbivora. Reasoning from this, Minkowski concluded that the blood should diminish in alkalinity in the latter, and has found this to be true of septic fever.

Scattered as the above is, it seems to the writer to offer a field for productive investigation. We know the reaction does change, has a normal value, cannot be without effect on the system, and have a ready means of determining the reaction.